REMARKS

Interview

Applicants wish to thank Examiner Kim for her time in conducting a telephonic interview on October 27, 2011 to discus the present grounds for rejection. The interview focused on the current ground for rejection under 35 U.S.C. § 102(b). In the interview the Examiner noted the lack of a required therapeutic effect on the brain was an important consideration in maintaining the current grounds for rejection. Applicants wish to thank the Examiner for her constructive feedback.

Amendments to the Claims

Claims 19, 20, 23, 25, 26, and 28-32 are pending in the present application, with claim 19 being independent. Applicant has amended Claims 19, 20, 23, 25, 26, 29, and 30. Applicant also has added new Claims 31 and 32 to provide an additional scope of protection commensurate with the original disclosure. Support for the new claims can be found, for example, on page 15, lines 32 to page 16, line 2. Additionally, Applicant has canceled Claims 21, 22, 24 and 27 herein without prejudice to or disclaimer of the subject matter recited therein. No new matter has been added.

Applicant has amended and canceled claims herein to remove issues from the pending claims, namely, that the original specification does not support features previously recited in those claims. Applicants disagree with the Examiner's objections and rejections based on those issues. Nevertheless, Applicants have removed those issues from the claims. Applicant has not acquiesced to any such rejections or objections and reserves the right to address the patentability of the relevant claim features in the future, in this or other related applications.

Amendments to the Specification

Applicant has amended the specification to replace the original title with a more descriptive title as requested by the Examiner.

Claim Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

In the Office Action dated July 6, 2011, the Examiner rejected Claims 19, 20, and 23-30 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement over the full scope of the claim. Applicants respectfully submit the amendments to the claims render the present grounds for rejection moot.

The Examiner acknowledges the claims are enabled for a method of enhancing antigenicity by administering supramolecular constructs comprising an antigenic peptide set forth in SEQ ID NOs: 1-6 with a modification, but does not enable for methods to increase memory restoration and curiosity awakening, treating Alzheimer's disease, multi-drug resistance in cancer cells or prion diseases comprising administering supramolecular antigenic constructs with GXXXGXXXGG or GXXXG peptide motifs.

The Examiner cites Taglianini *et al.* 77 JOURNAL OF VIROLOGY 8462 (2003) as evidence of a lack of effective therapy for prion diseases, and the lack of *in vivo* working examples related to the treatment of multi-drug resistance in cancer cells or prion disease as demonstrating a lack of enablement over the full scope of the invention. Applicants do not concede those arguments. However, in an effort to advance prosecution in the present application, Applicants have amended the claims to remove references to such methods of use. Applicants reserve the right to pursue such subject matter in one or more continuing applications. In light of the amendments to the claims, Applicants submit the Examiners above arguments are moot.

The Examiner further cites to Wolf-Klein *et al.* 24 AMERICAN JOURNAL OF HOSP PALLIAT CARE 77 (2007) (hereinafter Wolf-Klein), as evidence that no medical treatment is currently available to cure or stop the progression of Alzheimer's disease. As a threshold matter, lack of an existing treatment for a disease has no basis in our patent law as a sufficient ground for finding lack of enablement. Regardless, the presently claimed invention is directed to methods of restoring memory and curiosity awakening in Alzheimer's patients. Accordingly, Wolf-Klein's teachings regarding a lack of a complete cure are moot. Further, Wolf-Klein at least

acknowledges in the abstract of the article, the ability to successfully treat underlying symptoms regardless of the lack of an overall cure.

The present specification teaches that administration of supramolecular antigenic constructs according to the present invention in a mouse model (APPV171) of Alzheimer's disease resulted in significant levels of memory restoration and curiosity awakening. *Specification* at page 23, lines 16-22. These results are further supported and confirmed by a post-filing peer-reviewed journal article authored by the inventors, Muhs *et al.* 104 PNAS 9810 (2007). The article demonstrates increased memory improvement in an additional mouse model (APPxPS1 mice) of Alzheimer upon administration of a supramolecular antigenic construct according to the present invention ($A\beta_{1\text{-}15}$) that restored memory to levels comparable to healthy mice matched for age, gender, and genetic background. *See Muhs* at 9812 (top of second column) and 9813 (bottom of second column). A copy of the journal article is submitted herewith as Exhibit A. Accordingly, Applicants respectfully submit the presently claimed invention is enabled over the full scope of the invention. Finally, Applicants would like to note that the publication date of the Wolf-Klein article discussed above was prior to the publication of the Muhs article. Hence, whatever the conclusions of Wolf-Klein were, they were made without taking into consideration the results reported in Muhs.

For at least the foregoing, Applicants submit the present ground for rejecting claims 19, 20, and 23-30 under 35 U.S.C. § 112, first paragraph has been overcome and respectfully request it be withdrawn.

Written Description

In the Non-Final Office Action mailed on July 6, 2011, the Examiner further rejected claims 19, 20 and 23-30 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges that the specification does not show that Applicants were in possession of any supramolecular antigenic constructs comprising any unspecified amyloid peptide motifs including GXXXG and

GXXXGXXXGG or any fragments thereof. Applicants submit the amendments to the claims obviate the present ground for rejection.

In an attempt to further clarify the nature of the invention, claim 19 is amended herein to indicate that the antigenic peptide is β–amyloid or an active fragment thereof. β–amyloid is a well-known and well defined peptide within the art consisting of peptides 1-42 of the Amyloid Precursor Protein. The specification further provides examples of active fragments of the β–amyloid (e.g. SEQ ID NOs 1-5). Claims 29 and 30 specify that the β–amyloid fragment selected can have either a GXXXG or GXXXGXXXGG motif but does not indicate that the peptide can be a non β–amyloid peptide comprising GXXXG or GXXXGXXXGG. As noted in the Guidelines of the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement 66 Fed. Reg. 1099, 1106 (January 5, 2001), the written description requirement for a claimed genus (i.e. β–amyloid and active fragments thereof) may be satisfied through description of "a representative number of species, … and identifying characteristics, i.e., structure or other physical and/or chemical properties." *Id.* at 1106. A "representative number of species" means that the species which are adequately described are representative of the entire genus. *Id.* The fragments disclosed in SEQ IN NOs: 1-5 represent various fragments from over the entire length of the β–amyloid peptide. Claims 29 and 30 further define a shared structural feature of the genus. The members of the genus are not widely variant as they are limited to β–amyloid and immunogenic fragments that can be derived from the 42 amino acids of β–amyloid. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. *Fed. Reg.* at 1106. Accordingly, Applicants respectfully submit that one of ordinary skill in the art would recognize the Applicants were in possession of the presently claimed invention at the time of filing.

For at least the foregoing reasons, Applicants submit the ground for rejecting claims 19, 20 and 23-30 under 35 U.S.C. § 112, first paragraph has been overcome and respectfully request that it be withdrawn.

New Matter

In the Non-Final Office Action mailed July 6, 2011, the Examiner further rejected claims 19, 20 and 23-30 under 35 U.S.C. § 112, second paragraph as allegedly containing new matter. Applicants note that in the evaluation of the efficacy of antibodies to elicit changes in an animal behavior test (see Example 8) it is hard to imagine what reference point other than "prior to the administration of the supramolecular antigenic construct" could possibly be used. Accordingly, Applicants believe such disclosure is implicit. However, to further advance prosecution, Applicants have deleted the language at issue rendering the present ground for rejection moot. Applicants respectfully request the ground for rejection claims 19, 20 and 23-20 under 35 U.S.C. § 112, first paragraph (new matter) be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

In the Office Action mailed July 6, 2011, the Examiner rejected Claims 19, 20 and 23-30 under 35 U.S.C. § 102(b) as allegedly being unpatentable over Nicolau *et al.* 99 PNAS 2332 (2002) (hereinafter Nicolau). The Examiner has maintained the rejection for the reasons set forth in the Office Action mailed March 24, 2010. The Examiner contends that the method as previously claimed did not require a specific effect on the brain, and therefore in the present Office Action maintains that administration of supramolecular antigenic constructs in a non-Alzheimer mouse model is still representative of the patient population to be treated. *Office Action* at 9. Applicants submit the amendments to the claims overcome the present ground for rejection.

As noted above, claim 19 is amended to specify a method of restoring memory and curiosity awakening in a patient suffering from Alzheimer's disease and in need thereof. To qualify as an anticipatory reference, Nicolau must contain an enabling disclosure. *In re Hoeksema*, 399 F.2d 269 (CCPA 1968). A reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's

description of the invention with his [or her] own knowledge to make the invention." *In re Donahue*, 766 F.2d 531 (Fed. Cir. 1985). *See* M.P.E.P § 2121.

Nicolau does not qualify as an enabling reference under 35 U.S.C. § 102(a). As noted by Nicolau, the lack of a blood-brain barrier in the NORBA mouse model severely limits any conclusions that can be drawn about the ability to elicit a therapeutic effect on plaques in the brain. *Nicolau* at 2337 (first column, second full paragraph). Further, while Nicolau acknowledges that several mechanisms may be at play in explaining how antibodies elicited by the supramolecular antigenic constructs solubilize Aβ plaques, Nicolau also acknowledges the state of the art does not allow for a definitive conclusion. *Id.* (second column, second to last paragraph). Further, Nicolau notes their data suggest a strong role for direct interaction. "Finally, our own *in vitro* data (Fig. 4A) suggest that direct interaction of anti-Aβ antibodies with Aβ aggregates induces extensive solubilization of the latter." *Id.* (top of second column, underline added for emphasis). Therefore, in light of the evidence of extensive solubilization through direct interaction, Nicolau strongly suggests, or at least cannot exclude, the need to elicit an antigenic response across the blood-brain-barrier in order to have a potential therapeutic effect. Accordingly, Nicolau evidences a lack of knowledge in the art as to whether the ability to illicit an immunogenic response to Aβ in general is sufficient to establish the ability to elicit a therapeutic effect in the brain of Alzheimer patient. In addition, the experiments of Nicolau, owing to their inability to account for an effect across the blood-brain-barrier, do nothing to remedy this gap in the knowledge. Therefore, it can not be argued, per the standard set out in *Donahue*, that one of ordinary skill in the art could have combined Nicolau's description with their own knowledge to make the invention. Accordingly, Nicolau fails to provide an enabling disclosure and thus also fails as an anticipatory reference under 35 U.S.C. § 102.

For at least the foregoing reasons, Applicants submit the grounds for rejecting claims 19, 20 and 23-30 under 35 U.S.C. § 102(b) have been overcome and respectfully request that it be withdrawn.

No Waiver

All of Applicant's arguments and amendments are without prejudice or disclaimer. Applicant has not addressed each specific rejection of the independent and dependent claims because Applicant submits that the independent claims are allowable over the documents of record, as discussed above. Applicant has not acquiesced to any such rejection and reserves the right to address the patentability of any additional claim features in the future.

CONCLUSION

Applicant submits the foregoing as a full and complete response to the Official Action dated July 6, 2011. Applicant submits that this Amendment and Response places the application in condition for allowance and respectfully request such action. If any issues exist that can be resolved with an Examiner's Amendment or a telephone conference, please contact Applicant's undersigned attorney at 404.665.3099

Respectfully submitted,

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